

Please replace the paragraph at page 4, lines 29-33 with the following:

The antimicrobial of the invention may be prepared by heating poly(2-propenal, 2-propenoic acid) in the presence of the alcohol, preferably a polyol such as polyethylene glycol. Water is invariably present in the alcohols and it will be understood that the presence of at least some water assists in the nucleophilic reaction resulting in hemiacetal or acetal formation.

Please replace the paragraph at page 7, lines 4-12 with the following:

The poly(2-propenal, 2-propenoic acid) will generally contain no more than 10% on a molar basis of monomer units from monomers other than acrolein and is most preferably an acrolein homopolymer (before autoxidation). Where used other monomers may be selected from the group consisting of acrylic acid and vinyl pyrrolidone. The 2-propenoic acid groups are typically present in the amount of from 0.1 to 5 moles of carboxyl groups per kilogram. The poly(2-propenal, 2-propenoic acid) polymers typically have a number average molecular weight of over 1000 and most preferably over 2000. Typically the molecular weight is less than 10,000.

Please replace the paragraph at page 8, line 32 through page 9, line 2 with the following:

We have found that the antimicrobial of the invention has significantly improved activity in controlling gastrointestinal disease when compared with the poly(2-propenal-2-propenoic acid) from which it is prepared. The superactivated derivative of the present invention may be used to treat a wide range of animals (including humans) and a wide range of microbial infections.

Please replace the paragraph at page 9, lines 31-34 through page 10, lines 1-7 with the following:

We have found the antimicrobial of the invention to be effective against a wide range of microbes including protozoa, Gram positive bacteria and Gram negative bacteria. Of the Gram negative bacteria the antimicrobial of the invention has been found to

provide broad spectrum activity against coliforms or Enterobacteria. It is particularly useful in treatment of gastrointestinal diseases resulting from infection by *E. coli* such as enterotoxigenic *E. coli* and β -haemolytic *E. coli*. Colibacillosis is a devastating disease in the pig-rearing industry. The disease is generally associated with proliferation of β -haemolytic *E. coli* in the small intestine after weaning and gives rise to high mortality rates and morbidity rates in young weaner piglets and as a result, failure to make normal weight gains.

Please replace the paragraph at page 10, lines 24-29 with the following:

Clostridia are Gram positive bacteria responsible for serious disease in a range of animals. For example, necrotic enteritis is a disease known to affect commercial poultry. Clostridia produce exotoxins which are some of the most toxic of all known toxins. Necrotic enteritis particularly effects broilers of between 14 and 42 days of age. The condition causes pronounced apathy, diarrhoea and can cause death within hours.

Please replace the paragraph at page 11, lines 18-25 with the following:

In a preferred embodiment the concentrated composition of the antimicrobial is in a controlled-release form. The controlled release form will include the antimicrobial and a polymeric material for providing controlled release of the antimicrobial from the controlled-release system and is particularly useful in compositions for addition to solid feed material. As a result of the controlled release formulation the release of the antimicrobial may be delayed so as to occur mainly in the duodenum. A controlled release polymer may also minimise rejection of the composition due to taste or be used for rectal suppositories.

Please replace the paragraph at page 13, lines 16-34 with the following:

Solid forms for oral or rectal administration may contain pharmaceutically or veterinarianally acceptable binders, sweeteners, disintegrating agents, diluents, flavourings, coating agents, preservatives, lubricants and/or time delay agents. Suitable binders include gum acacia, gelatine, corn starch, gum tragacanth, sodium alginate, carboxymethylcellulose or polyethylene glycol. Suitable sweeteners include sucrose, lactose, glucose or flavonoid glycosides such as neohesperidine dihydrochalcone. Suitable disintegrating agents include corn starch, methylcellulose, polyvinylpyrrolidone, xanthan gum, bentonite, alginic acid or

agar. Suitable diluents include lactose, sorbitol, mannitol, dextrose, kaolin, cellulose, calcium carbonate, calcium silicate or dicalcium phosphate. Suitable flavouring agents include peppermint oil, oil of wintergreen, cherry, orange or raspberry flavourings. Suitable coating agents include polymers or copolymers of acrylic acid and/or methacrylic acid and/or their esters, and/or their amides, waxes, fatty alcohols, zein, shellac or gluten. Suitable preservatives include sodium benzoate, vitamin E, α -tocopherol, ascorbic acid, methyl parabens, propyl parabens or sodium bisulphite. Suitable lubricants include magnesium stearate, stearic acid, sodium oleate, sodium chloride or talc. Suitable time delay agents include glyceryl monostearate or glyceryl distearate.

Please replace the paragraph at page 15, lines 8-17 with the following:

In this application the antimicrobial composition of the invention may comprise further components. An antiseptic composition of the invention may be in the form of a lotion or product for washing such as a skin cleaner, soap bar or the like. Lotions are compositions which smooth or moisturize the skin. Lotions will preferably include an emollient. Examples of emollients include polyhydric alcohols such as glycerin, sorbitol, mannitol and propylene glycol and its homopolymers; fatty acid esters of monohydric alcohols such as isopropyl palmitate, isopropyl myristate and similar esters; polyol esters of fatty acids, ethoxylated lanolins, vegetable oils, mineral oils. Such compounds will be known to formulators of cosmetics.

Please replace the paragraph at page 16, lines 18-22 with the following:

Examples of non-ionic surfactants include but are not limited to alkyl polyglycosides, alcohol ethoxylates such as fatty alcohol ethoxylates and/or propoxylates, alkyl phenolethoxylates, glycol ester surfactants, PEG(20) sorbitan monooleate, polyethylene glycol cocoate, propylene oxide/ethylene oxide block polymers, alkanolamines, and so forth.

Please replace the paragraph at page 18, lines 16-19 with the following:

Examples of suitable isothiazolinones include 2-alkyl-4-isothiazoline-3-ones. Preferred isothiazolinones include 2-(n-octyl-4-isothiazolin-3-one), 4,5-dichloro-2-

B 12 cyclohexyl-3-isothiazolinone, 4,5-dichloro-2-(n-octyl-4-isothiazolin-3-one), 5-chloro-2-methyl-4-isothiazolin-3-one, and 2-methyl-4-isothiazolin-3-one.

Please replace the paragraph at page 18, lines 30-32 with the following:

B 13 The antimicrobial is useful with sunscreen agents such as aminobenzoates, salicylates, benzophenones, anthranilates, dibenzoylmethanes and camphor derivatives.

Please replace the paragraph at page 20, lines 15-18 with the following:

B 14 Henceforth, the process of providing increased antimicrobial activity by the formation of a new configuration of the subject polymers including poly(2-propenal, 2-propenoic acid), is referred to as "super-activation" and the polymers referred to as "super-activated polymers".

Please replace the paragraph at page 21, line 33 through page 22, line 4 with the following:

B 15 Dissolve sample with 1% by weight aqueous sodium bicarbonate to obtain the required concentration (unless specified to the contrary, 0.125% by weight of polymer). Weigh 19.9g of diluted sample into a sterile jar and inoculate with 0.1 mL of 10^7 - 10^8 cfu of *Ps.aeruginosa* and mix. At specified time-intervals, transfer 1 mL of inoculated sample to 9 mL of Lethen broth and vortex. Plate out serial 1 in 10 dilutions. Pour with trypticase soy agar. Incubate 3 days at 37°C.

Please replace the paragraph at page 22, lines 7-14 with the following:

B 16 The example describes a method of preparing poly(2-propenal, 2-propenoic acid) by oxidation of a solid acrolein polymer in air. This poly(2-propenal, 2-propenoic acid) is the preferred method of preparing a starting material for use in the method of the invention. Water (720 mL at ambient temperature, about 20°C) and acrolein (60g; freshly distilled, plus hydroquinone added to 0.25% w/w) were placed in an open beaker, within a fume cupboard, and very vigorously stirred, mechanically. Then, 0.2 M aqueous sodium hydroxide (21.4 mL) was added to bring the pH to 10.5-11.0.

Please replace the paragraph at page 26, lines 3-5 with the following:

B17 (a) 5% w/w solutions of polymers of a range of degrees of superactivation, apparent pH 5.7, were prepared similarly to example 2(a), but varying the percentage of PEG 200.

Please replace the Table 11(b) heading at page 30, line 17 with the following:

B18 Activity against *Pseudomonas aeruginosa*

Please replace the line at page 36, line 23 with the following:

B19 Group 1: No treatment (negative control).

Please replace the Table 14 heading at page 36, lines 28-30 with the following:

B20 PCR results of *Helicobacter spp.* using previously optimized genus specific primers where + represents a positive detection of *Helicobacter spp.* and - represents no detection.

Please replace the line at page 42, line 7 with the following:

B21 5) Polymeric antimicrobial 0.2% w/w + Glutaraldehyde 0.025% w/w

Please replace the paragraph at page 43, lines 1-3 with the following:

B22 It was shown that the acetal derivative of poly(2-propenal, 2-propenoic acid) was synergistic with Glutaraldehyde, EDTA, and Methyl Paraben, respectively versus *A. niger*, *C. albicans*, *E. coli*, *P. aeruginosa*, *S. aureus*.

Please replace the paragraph at page 43, lines 17-18 with the following:

B23 From each test tube 1 mL was subcultured into 9 mL recovery broth and vortexed well (NBT or Sabouraud + Tween 80 (SABT) or *A. niger*).